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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/064,512	07/23/2002	Loree Heller	1372.48	6625

21901 7590 07/29/2004

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/064,512	HELLER ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/23/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/23/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 1-11 are pending.

Election/Restrictions

Applicant's election of Group I (claims 1, 2, and 6-11) in the reply filed on 6/7/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3, 4, 5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/7/04.

Information Disclosure Statement

The information disclosure statement filed on 12/23/02 has been considered, but the articles were not initialed on the PTO-1449 because the articles are missing the name of the journal, the date and pages. See MPEP 809, 37 CFR 1.98. In order to have the articles initialed and dated on the PTO-1449, a new PTO-1449 properly citing the journal articles must be filed with the response to this office action. Failure to comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the non-complying information not being considered. See 37 CFR 1.97(i).

Drawings

The drawings were received on 7/23/02. These drawings are acceptable.

The petition for color drawings filed on 8/30/02 has been GRANTED.

Specification

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The disclosure is objected to because of the following informalities: The cross-reference section should be before field of invention section on page 1.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 6-8 were not examined under 112 first paragraph because the metes and bounds of the claims are not defined and were rejected under 112 second paragraph and the examiner cannot determine what the claims embrace.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 9-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a tumor *in vivo* comprising identifying an individual with a tumor; introducing by intra-tumoral injection at least one exogenous nucleic acid sequence; and applying an energy source to the tumor transfected with the exogenous nucleic acid sequence, does not reasonably provide enablement for a method of treating a tumor in vivo comprising introducing at least one exogenous nucleic acid to at least one tumor using a genus of administration routes and applying an energy source to the at least one exogenous nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the

quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention reads on a method of treating a tumor *in vivo* comprising identifying an individual with a tumor; introducing at least one exogenous nucleic acid to either the extracellular or intracellular space of a tumor in the individual; and applying an energy source to the at least one exogenous nucleic acid. The claimed invention lies in the field of cancer gene therapy.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (United States v. Technologies Inc., 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather a conclusion reached by many factors. These factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in In Re Wands (see above) and include the following:

Furthermore, and with respect to claims directed to any nucleic acid useful for gene therapy and directed to any treatment of an individual; the state of the art for gene therapy, exemplified by Anderson et al., *Nature*, Vol. 392, pp. 25-30, 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2).

In further view of the doubts expressed above by Anderson and Verma, the state of the art for cancer gene therapy as discussed by Vile et al., (Gene Therapy, Vol. 7, pp. 2-8, 2000). Vile teaches:

> The problems which gene therapy for cancer will take into the next millennium focus far less on the choice of therapeutic gene(s) to be used than on the means of delivering them. There is already a battery of genes that we know are very effective in killing cells, if they can be expressed at the right site and at appropriate levels. Nonetheless, until the perfect vector is developed, the choice of gene will remain crucially important in order to compensate for the deficiencies of the vectors we currently have available (page 2, 1st paragraph, left column). Whatever its mechanism, no single genes can be a serious contender unless it has a demonstrable bystander effect (page 2, right column). The requirement for such a bystander effect stems directly from the poor delivery efficiency provided by current vectors (page 2, right column).
>
> A genuine ability to target delivery systems to tumor cells distributed widely throughout the body of a patient would simultaneously increase real titers and efficacy. In truth, no such systemically targeted vectors exist yet. Injection of vectors into the bloodstream for the treatment of cancer requires not only that the vectors be targeted (to infect only tumor cells) but also that they by protected (from degradation, sequestration or immune attack) for long periods of time so that they can reach the appropriate sites for infection. Moreover, having reached such sites, the vectors must be able to penetrate into the tumor from the bloodstream before carrying out their targeted infection (page 4, bottom left column and top right column).

Thus, at the time the application was filed, the state of the art for gene therapy was considered highly unpredictable.

The claimed method reads on using any route for introducing at least one nucleic acid to at least one tumor. The unpredictability of the art is supported by the art of record; see Anderson, Verma, and Vile. The unpredictability involves poor and inefficient delivery of nucleic acid to target cells in vivo, host immune responses which limit the ability of the nucleic acid to infect target cells, uptake into other tissues instead of uptake into target tumor cells. The prior art teaches that the drug (e.g., nucleic acid) and electric pulses must be present and the specification does not teach one skilled in the art how to deliver the nucleic acid to at least one

tumor using a genus of administration routes so that the nucleic acid and electric pulse are present. See Heller et al. Advanced Drug Delivery 35: 119-129, 1999. The applicants teach injecting an empty plasmid directly into a tumor of a group of mice and applying an electrical pulse to the tumor (not the nucleic acid). The results obtained indicated that the group of mice treated with an empty plasmid followed by electrical treatment had reduced tumor volumes relative to other treatment groups. However, the relevance of this data to treatment of at least one tumor in an individual by delivering at least one nucleic acid using a genus of administration routes is unclear at best because neither the applicants nor the prior art provide a correlation or nexus between delivering a nucleic acid directly to a tumor in vivo such as the in the working example provided by applicants with results which the skilled artisan would reasonably expect to see in vivo using a genus of administrations. The teachings in the specification do not commensurate with the scope of the claims. The invention involves one of the most complex areas of medicine/molecular biology, gene therapy for the treatment of a tumor in an individual. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it is concluded that the skilled artisan would only have been enabled to use direct delivery of the nucleic acid to a tumor in vivo and would have need to have to conduct undue and excessive experimentation in order to practice the full scope of the claimed method using a genus of administration routes.

Furthermore, the claimed method reads on applying an energy source to at least one nucleic acid *in vivo*, wherein the nucleic acid is located extracellular to a tumor or in the intracellular space of a tumor. The applicants teach applying an energy source to a tumor comprising an exogenous nucleic acid. The prior art (Heller et al. supra) teaches applying an

energy source to a tumor *in vivo* transfected with a nucleic acid. Applicants do demonstrate that applying an electrical pulse to a tumor transfected with a nucleic acid results in reduction of the tumor size. The prior art teaches using an electric field to temporarily destabilize cell membranes in the presence of a drug (e.g., nucleic acid) to allow increased uptake of the drug into the cell. However, the relevance of applying an energy source to a tumor *in vivo* transfected with a nucleic acid to applying an energy source to a nucleic acid *in vivo* is unclear at best because neither the applicants nor the prior art provide a correlation or nexus between the results obtained in *in vivo* studies such as those provided by applicants with results which the skilled artisan would reasonably expect to see when applying an energy source to a nucleic acid *in vivo*. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered enabled.

In conclusion, the as-filed specification and claims coupled with the art of record at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable a method of treating a tumor *in vivo* comprising identifying an individual with a tumor; introducing by intra-tumoral injection at least one exogenous nucleic acid; and applying an energy source to the tumor transfected with the exogenous nucleic acid and does not provide sufficient guidance and/or factual evidence for one skilled in the art to practice the full scope of the claimed invention. Given that gene therapy wherein any carrier is employed to correct a disease or a medical condition in an individual was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to a gene therapy effect produced by any nucleic acid cited in the claims, one skilled in the art would have to engage in a large quantity of

experimentation in order to practice the claimed invention based on the applicants' disclosure and the unpredictability of gene therapy.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is rejected under 112 second paragraph because the claim does not define the active step for the phrase "wherein the energy source is adapted to make at least one cell in the at least one tumor". There is no nexus between the energy source and the cell in the tumor.

Claims 7 and 8 are rejected also under 112 second paragraph because the claims are dependent from claim 6.

Claim Rejections - 35 USC § 102

Claims 6-8 were not examined under 102 because the metes and bounds of the claims are not defined and the claims were rejected under 112 second paragraph.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
(f) he did not himself invent the subject matter sought to be patented.

Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Heller et al., (Melanoma Research 2000, 10, pp. 577-583).

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering a heterologous nucleic acid to at least one tumor and applying electroporation to the tumor comprising the nucleic acid. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Heller teaches administering a plasmid DNA to a tumor in mice and applying an electrical output to the tumor (pages 577-578).

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Monahan et al., (US 6,630,351).

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering a heterologous nucleic acid to at least one tumor and applying electroporation to the tumor comprising the nucleic acid. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Monahan teaches administering a compound comprising a heterologous nucleic acid and a polymer with a labile group to the intracellular and/or extracellular environment of a cell and applying electroporation to the cell, wherein the cell is a tumor in a subject (columns 4, 17, and 24).

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Maclaughlin et al. (US 2002/0102729).

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering a heterologous nucleic acid to at least one tumor and applying an electrical output to the tumor comprising the nucleic acid. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Maclaughlin teaches delivering a formulation comprising a heterologous nucleic acid to tumor cells in vivo and using electroporation on the cells to enhance delivery of the nucleic acid to the cells (pages 1 and 10-11).

Claims 1, 2, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicolau et al., (WO 97/07826).

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering a heterologous nucleic acid to at least one tumor and using electroporation on the tumor comprising the nucleic acid. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Nicolau teaches delivering a foreign nucleic acid to tumors in vivo and using electroporation on the tumors (pages 1 and 6-8).

Claim 11 reads on a method of treating a tumor in a subject comprising administering two heterologous nucleic acid to at least one tumor and using electroporation on the tumor comprising the nucleic acids. Nicolau teaches delivering foreign nucleic acids to tumor cells in vivo and using electroporation on the tumor cells comprising the nucleic acids (pages 1 and 3-8).

Claims 1, 2, and 11 are rejected under 35 U.S.C. 102(e) as being anticipated Heller et al., (US 6,714,816).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering a heterologous nucleic acid to at least one tumor and using electroporation on the tumor comprising the nucleic acid. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Heller teaches delivering nucleic acids to tumor cells in vivo and using electroporation on the tumor cells (columns 3 and 8-12).

Claim 11 reads on a method of treating a tumor in a subject comprising administering at least two heterologous nucleic acid to at least one tumor and using electroporation on the tumor comprising the nucleic acids. Heller teaches delivering nucleic acids to tumor cells in vivo and applying electroporation to the tumor cells (column 3).

Claims 1, 2, and 11 are rejected under 35 U.S.C. 102(e) as being anticipated Dev et al., (US 6,569,149).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1, 2, and 11 read on a method of treating a tumor in a subject comprising administering at least one heterologous nucleic acid to at least one tumor and using electroporation on the tumor. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Dev teaches delivering nucleic acids to tumor cells and using electroporation on the tumor cells (columns 14-18).

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated Heller et al., (US 6,135,990).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering at least one heterologous nucleic acid to at least one tumor and using electroporation on the tumor. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Heller teaches delivering nucleic acids to tumor cells and using electroporation on the tumor cells (column 3).

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated Gilbert et al. (US 6,314,316).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering a heterologous nucleic acid to at least one tumor and using electroporation on the tumor. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled. Gilbert teaches delivering nucleic acids to tumor cells and using electroporation (columns 2 and 3).

Claims 1, 2, and 11 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Heller et al., in US Patent 6,714,816 claim a method of delivering a charged molecule into a cell in vivo comprising placing a charged molecule outside and generally adjacent to the cell and using electroporation of the cell to cause the molecule to move into the cell. Although the claims do not specifically recite a nucleic acid as the molecule or the cell as a tumor cell, in view of the specification of '816 (See column 3-8), the claims read on the claims from the instant application. The claims from the instant specification are directed to delivering nucleic acids into a tumor cell in vivo using electroporation

Claims 1, 2, and 11 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Dev et al., in US Patent 6,569,149 claim a method of introducing molecules into cells of a tissue of a patient having a cell proliferative disorder using electroporation on the tissue, wherein the molecules are nucleic acids. The claims from the instant specification are directed to delivering nucleic acids into a tumor cell in vivo using electroporation.

Claims 1 and 2 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Heller et al., in US Patent 6,135,990 claim delivering a molecule into a target tissue using electroporation. Although the claims do not specifically recite a nucleic acid or a tumor, in view of the teachings in the specification '990 (column 3), the molecule can be a nucleic acid and the tissue can be a tumor. The claims from the instant specification are directed to delivering a nucleic acid into a tumor cell in vivo using electroporation.

Claims 1 and 2 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Gilbert et al., in US Patent 6,314,316 claim a method of delivering a bioactive molecule from an initial location to a target tissue comprising using electrodes to deliver the molecule to the target tissue. Although the claims do not specifically recite a nucleic acid or a tumor, in view of the teachings in the specification '316 (column 3), the molecule can be a nucleic acid and the tissue can be a tumor. The claims from the instant specification are directed to delivering a nucleic acid into a tumor cell in vivo using electroporation.

Claims 1 and 2 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Jaroszeski et al., in co-pending U.S. application 09/939,518 claim a method of delivery of a desired molecule into a target tissue comprising introducing a molecule into a target tissue and applying an electric field to the target tissue, wherein the target tissue is a tumor. In light of the teaching in the specification '518 (pages 6 and 8), the molecule can be a nucleic acid. The claims from the instant specification are directed to delivering a nucleic acid into a tumor cell in vivo using electroporation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, and 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,714,816. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application are directed to a method of treating a tumor in a subject comprising administering at least one heterologous nucleic acid to at least one tumor and using electroporation on the tumor and the claims from '816 recite a method for delivering a charged molecule into a cell in vivo comprising the steps of: positioning a charged molecule outside and generally adjacent to the cell in vivo, wherein the cell comprises a constituent of a tissue; delivering a first electromagnetic pulse to the cell having a strength and duration insufficient to cause electroporation of the cell and sufficient to cause an electromigration of the molecule toward the cell; delivering a second electromagnetic pulse to the cell having a strength and duration sufficient to cause electroporation of the cell, wherein at least one of the first pulse and the second pulse comprises an exponentially rising component. In light of the specification, a molecule can be nucleic acids and the tissue can be a tumor (column 3).

Claims 1, 2, and 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 3 of U.S. Patent No. 6,569,149. Although the conflicting claims are not identical, they are not patentably distinct from each other

because the claims from the instant application are directed to method of treating a tumor in a subject comprising administering at least one heterologous nucleic acid to at least one tumor and using electroporation on the tumor and the claims from '149 recite a method of applying an electric field to a tissue of a patient having a malignant cell proliferation disorder for the purpose of introducing a molecule into cells of the tissue to treat the disorder, wherein the molecule is nucleic acids.

Claims 1 and 2 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-28 of U.S. Patent No. 6,135,990. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application are directed to method of treating a tumor in a subject comprising administering at least one heterologous nucleic acid to at least one tumor and using electroporation on the tumor. The claims from '990 recite a method of applying an electric field to a tissue for the purpose of introducing a molecule into cells of the tissue. In addition, the claims from '990 teach delivering a molecule to the extracellular space of a tissue. The only differences between the claims of the instant application and the claims from '990 is that the claims from '990 do not recite wherein the tissue is a tumor and wherein the molecule is a nucleic acid. However, in light of the teachings in the specification, the specification defines the molecules as a nucleic acid and that the tissue can be a tumor (column 3).

Claims 1 and 2 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-15 of U.S. Patent No. 6,314,316.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from the instant application are directed to method of treating a tumor in a subject comprising administering at least one heterologous nucleic acid to at least one tumor and using electroporation on the tumor. The claims from '316 recite a method of applying an electric field to a tissue for the purpose of introducing a molecule into cells of the tissue. The only differences between the claims of the instant application and the claims from '316 are that the claims from '316 do not recite wherein the tissue is a tumor and wherein the molecule is a nucleic acid. However, in light of the teachings in the specification, the specification defines the molecules as a nucleic acid and that the tissue can be a tumor (column 3).

Claims 1 and 2 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 11, 45 and 51 of copending Application No. 09/939,518.

Claims 1 and 2 read on a method of treating a tumor in a subject comprising administering a heterologous nucleic acid to at least one tumor and using electroporation on the tumor. The step of identifying a subject with a tumor in the claims would be inherent to using the claimed method because the subject would have to have a tumor in order for the method to be enabled.

'518 claims using an electric field on a molecule to deliver the molecule into a tissue, wherein the tissue is a tumor. '518 further claims using jet injection to deliver the molecule to the tumor. The only difference between the claims of the instant application and the claims in '518 is that the instant application claims using a nucleic acid. However, in light of the

specification of '518, the only molecule used in the specification is a plasmid comprising a nucleic acid (pages 6 and 8).

This is a provisional obviousness-type double patenting rejection.

Claims 1, 2, and 11 are directed to an invention not patentably distinct from claims 1-14 of commonly assigned US patent 6,714,816. Specifically, the claims from the instant specification are directed to delivering nucleic acids into a tumor cell in vivo using electroporation and the claims from '816 are directed to a method of delivering a charged molecule into a cell in vivo comprising placing a charged molecule outside and generally adjacent to the cell and using electroporation of the cell to cause the molecule to move into the cell. In view of the teaching in the specification of '816, the charged molecule can be nucleic acids and the cell can be a tumor cell.

Claims 1, 2, and 11 are directed to an invention not patentably distinct from claims 1, 2, and 3 of commonly assigned US patent 6,569,149. Specifically, the claims from the instant specification are directed to delivering nucleic acids into a tumor cell in vivo using electroporation and the claims from '149 are directed to a method of introducing molecules into cells of a tissue of a patient having a cell proliferative disorder using electroporation on the tissue, wherein the molecules are nucleic acids.

Claims 1 and 2 are directed to an invention not patentably distinct from claims 17-28 of commonly assigned US patent 6,135,990. Specifically, the claims from the instant specification are directed to delivering nucleic acids into a tumor cell in vivo using electroporation and the claims from '990 are directed to delivering a molecule into a target tissue using electroporation.

In view of the teachings in the specification of '990, the molecule can be a nucleic acid and the tissue can be a tumor.

Claims 1 and 2 are directed to an invention not patentably distinct from claims 11-15 of commonly assigned US patent 6,314,316. Specifically, the claims from the instant specification are directed to delivering nucleic acids into a tumor cell in vivo using electroporation and the claims from '316 are directed to delivering a bioactive molecule from an initial location to a target tissue comprising using electrodes to deliver the molecule to the target tissue. In light of the teachings in the specification of '316, the molecule can be a nucleic acid and tissue can be a tumor.

Claims 1 and 2 are directed to an invention not patentably distinct from claims 1, 8, 10, 11, 18, 20, 21, 27, and 28 of commonly assigned US patent application 09/939,518. Specifically, the claims from the instant specification are directed to delivering nucleic acids into a tumor cell in vivo using electroporation and the claims from '518 are directed to delivery of a desired molecule into a target tissue comprising introducing a molecule into a target tissue and applying an electric field to the target tissue, wherein the target tissue is a tumor. In light of the teaching in the specification of '518, the molecule can be a nucleic acid.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned patent, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the

assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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